Attachment 6: Impact Statement (one-page limit): Upload as “Impact.pdf”.

Describe how the proposed research is relevant to ASD now. Detail the anticipated

outcome(s)/product(s) (intellectual and/or tangible) and/or improved understanding of

ASD that will be directly attributed to the results of the proposed research project (shortterm impact). Compare the anticipated outcomes from the proposed project to currently

available ASD information, products or treatments, if applicable. Describe the short-term

and long-term impact of the expected outcomes of the research projects on the ASD

community, individuals with ASD and their quality of life, and the well-being of their

families/caregivers.

The proposed project will investigate a novel and promising approach to treating autism. It is vitally important that non-pharmacological treatment strategies be developed, given that neurodevelopmental disorders are often highly sensitive to pharmacological treatments and prone to developing severe off-target side effects. Neurostimulation offers the advantage of being administered more focally, as in the case of high-definition tDCS, yielding a safer therapeutic modality associated with fewer adverse effects. Moreover, while some of the beneficial effects of pharmacotherapy are immediate, some of the desirable effects are gradual and may require weeks or months to develop. The efficacy of neurostimulation is more rapid than that of pharmacological interventions. In addition, understanding the underlying molecular processes that take place following neurostimulation has the potential to revolutionize this therapeutic strategy, as this will provide the knowledge necessary to enhance the efficiency of neurostimulation by investigating the effects of unique and focused stimulation protocols with regard to current intensity, length, and frequency of treatments and comparison between types of neurostimulation, such as direct current-based (tDCS), alternating current-based (tACS), and random noise-based (tRNS) strategies.

Although outside the immediate scope of this study, molecular knowledge will provide more accurate readout assays for investigating additional neurostimulation parameters, such as the optimal stimulation frequency for tACS. Additionally, knowledge of the underlying molecular mechanisms will enable the implementation of pharmacological augmentation therapies that will enhance neurostimulation efficiency. The anticipated outcomes of the study will ideally improve cognitive deficits, social deficits, and motor dysfunction in our AS model mice. All of these deficits and impairments are present in human AS patients and are also shared with multiple other neurodevelopmental disorders. The major cognitive, behavioral, and motor aspects that we intend to examine are related to memory deficits, anxiety features, motor function, and aggression. We and others have firmly established the presence of these behaviors in AS, and we have extensive experience in conducting the experiments necessary to test these behaviors in mice. Therapies that can improve the memory and cognitive functioning of patients with autism will improve the learning curve for these individuals, better equipping them to adapt to novel environments and novel situations. Many of the maladaptive behaviors observed in children with autism are due to cognitive behavioral rigidity. Enabling these children to be more flexible and learn new coping strategies will significantly improve their quality of life and will make them less dependent on their caregivers. Neurostimulation can similarly impact motor function, which is noteworthy given that many children with autism suffer from clumsiness or other limitations to their coordination and fine motor skills. Neurostimulation holds great promise as a means of overcoming these deficits, improving the independence of treated children. Another extremely beneficial aspect that is relevant for caregivers is the mitigation of aggression. Many neurodevelopmental disorders are accompanied by bouts of aggressive behaviors, especially when under stress. This unexpected aggression is one of the major hardships for caretakers. Lessening anxiety and aggressive behavior via neurostimulation is a promising therapeutic strategy for the treatment of children suffering from neurodevelopmental disorders, providing invaluable relief to their caregivers.